Remarks

I. Support for Amendments to the Claims and Specification

A. Specification Amendment Support

The description for Figures 10 and 11 have been amended to insert SEQ ID NOs for the depicted amino acid sequences. The SEQ ID NOs for the sequences disclosed in those Figures correspond to the SEQ ID NOs contained in the substitute sequence listing, submitted herewith. These amendments do not constitute new matter.

Applicants respectfully request that the substitute sequence listing be incorporated into the application, replacing the prior-filed version of the sequence listing. The substitute sequence listing merely adds SEQ ID NOs 80-84, which were present in Figures 10 and 11 as filed, but were inadvertently unidentified by SEQ ID NO. The substitute sequence listing does not go beyond the application as originally filed, and does not contain new matter.

B. Claim Amendment Support

The claims are amended as noted above. In particular claims 3-9, 11-31, 39-45, 47-56, and 60-61 are canceled. In particular, claims 3-4, 6-9, 12-31, 39, 41, 43, 45, and 60-61 were previously pending as withdrawn as relating to patentably distinct subject matter (see Restriction Requirement, mailed June 29, 2005) and are now canceled without prejudice to their refiling in a timely filed divisional or continuing application. Claims 1, 2, 10, 32, 34-38, 46, and 57-59 have been amended. New claims 62-81 have been added. Support for the claim amendments and new claims can be found throughout the specification, for example, in the originally filed claims, Figs. 1-4, ¶¶ [0050]-[0054], [0081]-[0082], [0112]-[0114], [0158]-[0172], and the Examples (with Example 1, beginning at ¶ [0265]) of the application as published (U.S. Published Patent Application Number 2004/0097712). Support for the amendments to Claims 1 and 2 (i.e., inserting the recited SEQ ID NOs) can be found at, for example, Figures 10 and 11; the revised sequence listing, submitted herewith; and Example 6 (*e.g.*, pg. 78, ll. 6-29; and pg. 82, ln. 10 – pg. 83, ln. 5). The amendments do not constitute new matter.

Without acquiescing to the propriety of the pending rejections, the amendments to the claims are made in order to provide proper antecedent basis, clarify the claim language, remove subject matter drawn to non-elected, patentably distinct subject matter (see, Restriction Requirement, mailed June 29, 2005 and Office Action, mailed October 11, 2005), and to expedite

prosecution of the claimed subject matter. Applicants expressly reserve the right to pursue the subject matter of the canceled claims in future divisional or continuing applications.

II. Claim Rejections -- 35 USC §112, first paragraph, enablement

Claims 1, 2, 5, 32-38, 40, 42, 44, 46-49, and 52 stand rejected under 35 USC §112, first paragraph are rejected for allegedly failing to reasonably enable all of the embodiments encompassed by the claims. Applicants respectfully traverse this rejection.

MPEP § 2164.01(a) states that in order to satisfy the enablement requirement, an applicant must enable one of ordinary skill in the art to make and use the claimed invention. A determination of whether claims are adequately enabled are guided by the "Wands factors" which include: (1) the quantity of experimentation required, (2) the amount of guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims. *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988). Importantly, enablement is not precluded by the necessity of even a considerable amount of experimentation in some cases, particularly if the experimentation is routine in nature, and when the invention falls within an unpredictable art class. *U.S. v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988); *Ex Parte Mark,* 12 USPQ2d 1904(BPAI 1989); *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). Moreover, some unpredictability of the outcome of experimentation does not make the experimentation undue since an experiment would hardly be done if its outcome was known beforehand. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976).

Applicants respectfully assert that the full scope of the claims, as pending before the above amendments and as now pending, are fully enabled in light of the disclosure provided by the specification.

A. Claims 1, 2, 5, 32-38, 40, 42, 44, 46-49, and 52

The Action specifically alleges that the claims are not enabled for antibodies comprising less than the complete light and heavy chain variable domains, and/or antibodies comprising at least 90% identity to a recited sequence, and relies on several references for support of that assertion, including Rudikoff et al., (PNAS USA, (1982), 79:1979-1983), Colman (Research in Immunology,

(1994), 145:33-36), in view of Janeway et al., *Immunobiology,* 5th Ed., pp. 94-105. Applicants respectfully traverse this rejection.

Applicants' position regarding enablement of the original claims is of record, and incorporated by reference herein. As indicated above, Applicants have amended the claims to expedite prosecution without aquiescing to the propriety of the rejections pending in the current Action. Accordingly, insofar as this rejection relates to now canceled claims 5, 40, 42, 44, 47 to 49 and 52 it is now moot.

Certain of the pending claims relate to antibodies that comprise 3 CDR regions of the light chain and of the heavy chain of the claimed antibody or the heavy chain variable region of SEQ ID NO 80 or the light chain variable region of SEQ ID NO 81, or both. In view of the following, Applicants respectfully submit that claims directed to antibodies comprising three CDR regions of the light chain and of the heavy chain, or either the heavy chain variable domain of SEQ ID NO:80 or the light chain variable region of SEQ ID NO:81 are enabled. This position is supported by at least the following disclosure in the specification.

1. Applicants have provided guidance describing the preparation of IL-1R1 antibodies including description of the antigen.
2. Applicants produced an antibody that binds IL-1R1 that contains a variable heavy chain of SEQ ID NO: 80 and a variable light chain of SEQ ID NO:81.
3. Applicants disclose humanization of antibodies and chimaeric antibodies in the specification.
4. Applicants provide examples of anti-IL-1R1 activity.
5. One of skill in the art at the time the application was filed should be able to produce antibodies that bind IL-1R1 by screening a library using the specific VL (or VH) described in Applicants' application to find a complimentary variable domain.

Based on at least the above disclosure, claims to an antibody with a defined heavy or light chain variable region are enabled because the Applicants' disclosure of an antibody that binds IL-1R1 comprising a defined VH or VL sequence would provide enough structure for one skilled in the art to practice such claims. Furthermore, the above support parallels the support suggested necessary to justify enablement of such claims, as set forth in the public guidance provided by SPE Larry R. Helms. (See Appendix A, included with this response). This guidance as applied to the

application indicates that claims such as those now pending (for example claims 1, 2, 10, 46, and 64-69) would be enabled when the specification contains disclosure including: (a) IL-1R1 from human tissue (see, *e.g.,* Example 1, Example 5 (pp. 76-77); (b) an antibody that binds IL-1R1 and contains the recited SEQ ID NOs including a heavy chain variable region and/or a light chain variable region, and (see, *e.g.,* Table 2 and Examples 5 and 6); and (c) disclosure of humanized and chimeric antibodies (see, *e.g.,* pg. 35-36, Example 1). Applicants contend that based on the requirements laid out by Mr. Helms, the claims are enabled.

Futhermore, contrary to the position set forth in the Action, the Janeway reference does not teach that all heavy and light chain CDRs are required for antigen binding function. When read in its entirety, Janeway in fact teaches (and exemplifies) that in some cases, less than all CDRs make contact with the target antigen (*see,* Fig. 3.8a caption: "Seven amino acid residues of the antigen...are bound in the antigen-binding pocket. Five of the six CDRs...interact with the peptide."). Thus, the art recognizes (and Janeway teaches) that variability can exist between antigen-antibody/specific binding agent interaction, and that every case *does not require* that all six CDR regions interact with the target antigen in order for the antibody or specific binding agent to have binding activity. Applicants incorporate the arguments made in prior responses to Office Actions relating to the enablement requirement, and maintain that the disclosure in the application is sufficient to at least reasonably enable one of skill in the art to make and use the full scope of the invention in the original claims, and as now recited in the pending claimed.

Applicants wish to note for the record that while they may not have addressed each and every argument raised by the Examiner in the enablement section of the office action, this should not be construed as acquiescence with those arguments. It was deemed unnecessary to address each point because based on the above argumentation, the claim amendments and claim cancellations, the additional arguments made by the Examiner are believed moot.

In light of the above reasoning, Applicants believe that the claims are fully enabled given the amount of guidance provided in the specification. Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

III. Claim Rejections -- 35 USC § 112, first paragraph, written description

Claims 1, 2, 32-38, 40, 42, 44, 46-49, and 52 stand rejected as failing to comply with the written description requirement. The Action asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably covey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 112, first paragraph, all that is required to satisfy the written description requirement is that the specification describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991); M.P.E.P § 2163(I). Possession is shown "by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention." M.P.E.P. § 2163.02 (citing *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir.1997)).

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. M.P.E.P. § 2163(I)(A) (citing *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976)). Thus, a description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See, e.g., In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971); M.P.E.P. § 2163.04. Therefore, the Office must have a reasonable basis to challenge the adequacy of the written description and has the initial burden of presenting, by a preponderance of the evidence, why a person skilled in the art would not recognize in an Applicant's disclosure a description of the invention defined by the claims. *See, e.g., In re Wertheim*, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976); M.P.E.P. § 2163.04.

Claims 1, 2, 32-38, 40, 42, 44, 46-49, and 52 stand rejected for allegedly failing to satisfy the written description requirement because the claims recite, or depend from claims which recite, antibodies comprising less than the complete light and heavy chain variable domains. Applicants respectfully disagree with this basis of rejection. As indicated above Applicants have amended the claims to expedite prosecution without aquiescing to the propriety of the rejections in the pending

Action. Accordingly, insofar as this rejection relates to now canceled claims 40, 42, 44, 47-49 and 52 it is now moot.

Contrary to the Office's position, the Applicants have disclosed relevant identifying characteristics of the specific binding agents of the invention, including structural (*e.g.*, CDR regions, epitope binding data), physical, and chemical properties (*e.g.*, sequence description) which demonstrate a clear possession of the invention, in its full scope. As noted by the Office, Applicants have disclosed amino acid sequence information for five IL-1R1 antibodies (*e.g.*, ¶ [0278], Figures 1-11, and revised sequence listing submitted herewith); identified the complementary determining regions within the variable light chain and variable heavy chain sequences of those antibodies (*e.g.*, Figures 10-11); and have provided epitope mapping data for antibodies (see, *e.g.*, Examples 5 and 9; Figures 17-21 and 23-25). As the Office has acknowledged, the skilled artisan recognizes that CDR regions have been identified as important in antigen binding and recognition, and can be used to generate other similarly functioning antibodies/antibody fragments. These would include sequences such as, for example, single chain Fv, Fab, F(ab'), and active peptides comprising CDR regions. While the Office appears to impose a requirement that Applicants must, in an application, present data for every embodiment encompassed by the claims, this is clearly not and has never been the standard under § 112. Indeed, one of skill in the art would be able to envision fragments, deletions, insertions, and substitutions to the amino acid sequence of the exemplified sequences as well as sequences having a certain percentage identity to the exemplified sequences.

In light of the argument above and the amendments to the claims made to expedite prosecution of the application, Applicants submit that one skilled in the art would recognize, at the time the application was filed, that the inventors had possession of the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph.

IV. Claim Rejections -- 35 USC § 102(e)

Claims 55 and 56 stand rejected under 35 USC §102(e) as being anticipated by Dower, US Patent No. 6,511,665 (the '665 patent) as evidenced by Vigers *et al.* While Applicants respectfully disagree with the basis of this rejection, nonetheless as indicated above, Applicants have amended the claims to expedite prosecution without aquiescing to the propriety of the pending rejections.

Insofar as this rejection relates to now canceled claims 55 and 56, Applicants believe the rejection is now moot.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

V. Claim Rejections -- 35 USC § 103(a)

Claims 55 and 56 stand rejected under 35 USC §103(a) as being unpatentable over Dower et al. (US Patent No. 6,511,665) as evidenced by Vigers et al. and Schreuder et al. While Applicants respectfully disagree with the basis of this rejection, nonetheless as indicated above, Applicants have amended the claims to expedite prosecution without aquiescing to the propriety of the pending rejections. Insofar as this rejection relates to now canceled claims 55 and 56, Applicants believe the rejection is now moot.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

VI. Claim Objections

Claims 10 and 53 are objected to; claim 10 for depending from rejected claim 5, and claim 53 for depending from rejected claim 46 and for reciting SEQ ID NOs not included in elected Group III. The Action indicated that claim 10 would be allowable if rewritten in independent form. The Action also indicated that claim 53 would be allowable if rewritten in independent form and such that it only recites the elected SEQ ID NOs. Claim 10 has been amended to independent form. Claim 46, has been amended to incorporate all the limitations of claim 53 and such that it only recites the elected SEQ ID NOs. Accordingly, Applicants respectfully request that the claims be allowed.

VII. Conclusion

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

The Examiner in charge of this application is invited to contact the undersigned representative as indicated below if it is believed to be helpful.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

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By: /Christopher P. Singer/
Christopher P. Singer
Reg. No. 48,701

Phone: 312-913-0001
Fax: 312-913-0002